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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/917,800	07/31/2001	Donna L. Mendrick	044921-5038	1108

9629 7590 05/02/2003

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EXAMINER

LY, CHEYNE D

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 05/02/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/917,800

Applicant(s)

MENDRICK ET AL.

Examiner

Cheyne D Ly

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on March 05, 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 55-91 is/are pending in the application.
- 4a) Of the above claim(s) 90 and 91 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 55-89 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 55-91 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3,8,9,13.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

1. Applicant's election with traversal of claims 55-89, alpha-naphthylisothiocyanate (ANIT) as the toxin and liver as the tissue, in Paper No.12, filed March 05, 2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
2. It is acknowledged that Applicants have cancelled claims 1-54 and withdrawn claims 90 and 91.
3. Claims 55-89, alpha-naphthylisothiocyanate (ANIT) as the toxin and liver as the tissue, are examined on the merits.

Claim Objections

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (Page 32, Lines 31-32 to page 33, lines 1-6). Applicant(s) is/are required to delete the embedded hyperlink and/or other form of browser-executable code, or inactivate the hyperlink. See MPEP § 608.01.

Information Disclosure Statement

5. The foreign patent documents in Paper No. 3, filed October 11, 2001, have not been considered because the patent documents are not in the instant application.

Priority

6. In order for the present application to receive benefit of priority for an invention to an earlier application, the earlier application (the parent or provisional application) must disclose the invention so as to be sufficient to comply with the requirements of the first paragraph of 35

U.S.C. 112 regarding said invention. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ 2d 1077 (Fed. Cir. 1994). It is acknowledged that the specific claimed subject matter of the present application was disclosed in the priority document (US 60/290645) with a priority date of May 05, 2001. Therefore, the claim for domestic priority under 35 U.S.C. §119(e) has been established to be May 05, 2001.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 55-89 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claims 55, 86, and 88 are regarded as vague and indefinite because the metes and bounds of the claimed method are unclear. The active steps of the claims comprise of preparing and comparing gene expression profiles while the preamble recites a method of predicting a toxic effect. Which component, the preamble or the active steps, of the claims control the metes and bounds of these claims? Currently, it is inconclusive as to which component is controlling the metes and bounds of these claims. Claims 56-85, 87, and 89 are rejected from being directly or indirectly dependent from claims 55, 86, or 88.

10. Specific to claims 55, 86, and 88, step (b), the phrase “comparing the gene expression profile to a database” causes the claims to be vague and indefinite. The step of comparing is unclear because it is uncertain what is being compared in step (b). Is the comparison in step (b) comparing expression profile to the whole database or to a specific data set contained within the

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database? Clarification of the metes and bounds of the claims are required. Claims 56-85, 87, and 89 are rejected from being directly or indirectly dependent from claims 55, 86, or 88.

11. Specific to claims 58-61, line 2, the term "that's" causes the claim to be vague and indefinite. While applicant may be his or her own lexicographer, a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See *In re Hill*, 161 F.2d 367, 73 USPQ 482 (CCPA 1947). The term "that's" in claim 58-61 is used by the claim to indicate expression belongs to a gene, while there is not accepted meaning for the term "that's."

Clarification of the metes and bounds of the claims are required.

12. Specific to claims 61 and 71, line 3, the phrase "protein adduct former" causes the claim to be vague and indefinite. The phrase is unclear because "former" is a reference term. The claims lack antecedent basis for the item being referred to by the claims. Clarification of the metes and bounds of the claims are required.

13. Specific to claim 76, lines 2 and 3, the phrase "external" database causes the claim to be vague and indefinite. It is unclear what criteria are being used to consider that a database is external (external of the USPTO or external to the Applicants' office). Clarification of the metes and bounds of the claims are required.

14. Specific to claim 81, line 2, the term "measures" causes the claim to be vague and indefinite. It is unclear how information can actively measure the ability of a gene to accomplish a specific task. Clarification of the metes and bounds of the claims are required.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

16. (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

17. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 55-60, 62-70, 72-76, 78, 79, 81, and 84-88 are rejected under 35 U.S.C. 103(a) as being unpatentable over Friend et al. (US 6218122 B1) taken with Cunningham et al. (US 6372431 B1).

19. Friend et al. discloses a method for predicting response profiles (expression profile) to toxins by measuring a plurality of cellular constituents that indicate aspects of the biological state of a cell (column 9, lines 15-38), as in claim 81. Expression profile data are loaded into the computer system, which cause the execution of expression profile analysis software to determine the difference between diagnostic profile, and a response profile determined from the perturbation response profile data contained in a database (columns 13, lines 45-55 and 19, lines

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17-38), as in claims 55, step (b), 57, 75, 78, 79, and 86-88. The method of Friend et al. discloses that expression profiles were established for approximately 6000 genes (column 10, lines 40-42). The differential expression of the 6000 genes exposed to a drug (column 11, lines 40-45), as in claims 64-67, 73, and 74. The above disclosures describe the limitations of claims 68.

Microarrays were prepared with probes generated by PCR reactions (column 22, lines 37-51), as in claim 70. Two different cells are hybridized to the microarray; one cell type exposed to a drug or toxin another not exposed to a drug or toxin (control) (column 21, lines 52-56), as in claim 69.

20. However, Friend et al. does not disclose that the toxin is an ANIT or an external database practice.

21. Cunningham et al. discloses a method for screening compounds and therapeutics for metabolic responses indicative of a toxic compound or molecule (Abstract) such as hepatoxin (column 7, line 43-50), as in claim 85. The toxic compounds may include ANIT affecting the liver (column 2, lines 1-8), as in claims 55, step a), 56, and 72. Tables 1-10 disclose differential expression of genes correlated to liver pathology, as in claim 58. The fluorescence signal within each element was then integrated to obtain a numerical value corresponding to the average intensity of the signal (column 24, lines 15-19), as in claims 62 and 63. The ESTs are derived from the ZOOSEQ database (column 9, lines 14-16), as in claim 76. Acetaminophen is a widely-used analgesic which is metabolized by specific cytochrome P450 isozymes with the majority of the drug undergoing detoxification by glucuronic acid, sulfate and glutathione conjugation pathways (column 1, lines 37-40), as in claim 84.

22. Clearly, a skilled artisan would have been motivated to partake the concept emphasized by Friend et al., a method of using expression profiles for early diagnosis or prognosis or

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determination of the level of a disease state which may be resulted from exposure to a toxin (column 6, lines 49-54); and improve on the said method by including expression profiles of toxicological responses to the toxin, ANIT, as taught by Cunningham et al. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to use the method of Friend et al. for predicting response profiles (expression profile) to ANIT as taught by Cunningham et al.

CONCLUSION

23. NO CLAIM IS ALLOWED.

24. Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (703) 308-3880. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

26. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028.

27. Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina Plunkett, whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

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C. Dune Ly

4/29/03

Ardin H. Marschel
ARDIN H. MARSCHEL
PRIMARY EXAMINER